antibiotic cocktail pretreatment at the end of experiment)(IDDF2021-ABS-0196 Figure1B. *Clostridium butyricum* and its supernatant ameliorated colitis and regulated immune cells; The macroscopic images of colon)(IDDF2021-ABS-0196 Figure 1C. *Clostridium butyricum* and its supernatant ameliorated colitis and regulated immune cells; The statistical analysis of colon length). The results of qPCR showed that the relative expression of pro-inflammatory cytokines TNF- α , IL-6, IL-1 β , IL-17a were down-regulated after CBM and its supernatant treatment. And the relative expressions of anti-inflammatory cytokines TGF- β , IL-10, IL-4, IL-5, IL-13 were up-regulated (IDDF2021-ABS-0196 Figure1F. *Clostridium butyricum* and its supernatant ameliorated colitis and regulated immune cells; The amount of Th1 cells based on flow cytometry, and its statistical analysis). Flow cytometry showed that the amount of neutrophils, macrophage, Th1, Th17 cells were down-regulated which were the pro-inflammatory immune cells in intestinal mucosa lamina propria after CBM and its supernatant treatment (IDDF2021-ABS-0196 Figure1D. *Clostridium butyricum* and its supernatant ameliorated colitis and regulated immune cells; The amount of neutrophil based on flow cytometry, and its statistical analysis) (IDDF2021-ABS-0196 Figure1E. *Clostridium butyricum* and its supernatant ameliorated colitis and regulated immune cells; The amount of macrophage based on flow cytometry, and its statistical analysis) (IDDF2021-ABS-0196 Figure1F. *Clostridium butyricum* and its supernatant ameliorated colitis and regulated immune cells; The amount of Th1 cells based on flow cytometry, and its statistical analysis) (IDDF2021-ABS-0196 Figure1G. *Clostridium butyricum* and its supernatant ameliorated colitis and regulated immune cells; The amount of Th17 cells based on flow cytometry, and its statistical analysis) (IDDF2021-ABS-0196 Figure1H. *Clostridium butyricum* and its supernatant ameliorated colitis and regulated immune cells; The relative expression of inflammatory cytokines)

Conclusions CBM can alleviate the symptoms and colon shortening of mice with colitis after pre-treatment with ABx, improve the expression of inflammatory factors, and might play an anti-inflammatory role by down-regulating the infiltration of inflammatory immune cells in intestinal mucosa lamina propria.

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DELAYED INTERVENTION OF AGAROPECTIN-DERIVED OLIGOSACCHARIDES ALLEVIATE LIPID ACCUMULATION BY MODULATING INTESTINAL FLORA HOMEOSTASIS

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Background Polysaccharides from marine red algae possess a variety of biological activities. And, our previous study

illustrated that the agaropectin-derived oligosaccharides from *Gloiopeltis furcata* (SAOs) activated AMPK signaling pathway in vitro. However, the effects of SAOs on alleviating lipid accumulation in vivo and its underlying mechanism are not clear.

Methods C57BL/6J mice were randomly divided into five groups of ten mice each. Control group: mice were fed a normal chow diet. And, the other four groups were continuously fed an HFD for 24 weeks to establish the obesity model. After 24 weeks, the Metf, SAOs-L, and SAOs-H groups received either metformin (225 mg/kg/d dissolved in saline) or SAOs (100 or 300 mg/kg/d dissolved in saline), while the Control and Model groups were given aliquots of saline. Saline and the drugs were given by oral gavage for the final six weeks of the experimental period.

Results We found that SAOs decreased the body weight (about 3 grams) and the adiposity index (from 7 to 5) after a 6-week treatment. In addition, SAOs alleviated lipid accumulation in the liver, perirenal fat, and epididymal fat tissues. Investigation of the underlying mechanism showed that the cecal microbiota dysbiosis in HFD-fed mice were ameliorated after SAOs treatment, including significantly increasing the relative abundance of *Alistipes*, while reducing the relative abundance of *Helicobacter*. In addition, Spearman's correlation analysis indicated that changes in the cecal microbiota could regulate lipid accumulation, oxidative stress, inflammation.

Conclusions The present study confirmed that SAOs could effectively alleviate HFD-induced fat accumulation, partly through regulating cecal microbiota by fostering the preferential growth of probiotics and suppressing the relative abundance of harmful bacteria. In summary, our study illustrated that SAOs could be further developed as a potential pharmaceutical agent for obesity.

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CANAGLIFLOZIN ALLEVIATES DIABETIC CARDIOVASCULAR DISEASE VIA LIPID LOWERING, MITOCHONDRIAL HOMEOSTASIS, AND GUT MICROBIOTA REGULATION

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Background T2DM is associated with CVD. SGLT2i represent the most effective class of oral medications for the treatment of T2DM, and have been shown to improve generalized vascular dysfunction.

Methods T2DM was induced by HFD to male C57BL/6J mice for 24 weeks. After that, HFD-fed mice were treated with Cana (50 mg/kg/d) by oral gavage for 6 weeks. Myocardial mitochondrial morphology and cardiovascular abnormalities were assessed by TEM, immunofluorescence staining and Masson's staining; lipids profile and oxidative stress state were assessed by corresponding biochemical assay kits and immunohistochemical staining; the myocardial injury was characterized by H&E staining, TUNEL, and ELISA assays; colonic gut microbiota was assessed by 16S rDNA sequencing.

Results Cana reduced the lipid (such as TG, TC, and LDL-C) accumulation in serum, thus decreased atherogenic index of plasma and arteriosclerosis index values. More importantly, Cana decreased the thickness of the vascular basement membrane, improved cardiac mitochondrial homeostasis, and relieved oxidative stress (e.g. regulation of ROS, SOD, GSH, and MDA levels). And, Cana reduced the circulating markers of inflammation (such as TNF α , MCP-1, and IL-6). Myocardial injury was alleviated after Cana treatment with decreasing levels of serous cTn I (from 95 pg/mL to 75 pg/mL) and sCD40L (from 120 pg/mL to 90 pg/mL). Thus, the cardiovascular abnormality was relieved by elevating the CD31 expression level and suppressing fibrosis and basement membrane thickening (from 0.6 μ m to 0.2 μ m) in T2DM mice. Interestingly, Cana administration increased the ratio of Firmicutes/Bacteroidetes (from 230% to 98%) and the relative abundance of Olsenella, Alistipes, and Alloprevotella, while decreasing the abundance of Helicobacter and Mucispirillum in mice with diabetic CVD.

Conclusions Cana treatment improved CVD by decreasing the risk of atherosclerosis and reducing the thickness of the vascular basement membrane. Importantly, Cana treatment significantly elevated myocardial mitochondria homeostasis, thus ameliorated the oxidative stress and inflammatory states. Moreover, Cana subtly altered microbiota composition in T2DM mice with CVD, which contributed to the improvement of CVD. Collectively, the improvements of myocardial mitochondrial and gut microbiota homeostasis, may represent an important mechanism underlying the cardiovascular benefits of Cana treatment.

IDDF2021-ABS-0199 REVEALING MOLECULAR AND CELLULAR DISCRIMINANTS OF TYPE 2 DIABETES BY INTEGRATIVE ANALYSIS OF PANCREATIC SINGLE-CELL RNA-SEQ DATA

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Background Type 2 diabetes (T2D) cause the dysfunction of insulin produced in the pancreas by beta cell, which leads to the non-correct response in fat, liver, and muscle cells. However, we are still far from completely understanding the molecular and cellular discriminants for T2D on cell level.

Methods On collected and integrated single-cell RNA-Sequencing (scRNA-seq) data from 3 publicly available pancreas datasets, we have trained an interpretable deep neural network model, which can provide an efficient T2D classifier to estimate the cell states from normal or T2D individuals and selected the key genes. Next, these key genes were used as anchors in down-stream analysis. Then, the cell type, marker gene, gene activity in cells, and cell-cell communications were all extracted and used in estimating the cell-type proportions and cell-type specific differential expressions in individual-matched bulk sequencing data.

Results We trained and tested T2D classifier to predict the states of cells from multiple single-cell datasets, and acquired significantly high accuracy (ACC=0.9034) in independent

validation. Among key genes ranked by our classifier, there were 4, 12, 63 differentially expressed genes between normal and T2D states detected in acinar, alpha and beta cells, suggesting the stronger signal of dysfunction of T2D-relevant beta cells than other types of cells. These genes are significantly correlated with metabolic processes relevant to abnormal metabolism of T2D, and mainly show loss of expression, activity, and signaling changes among cell-cell communication in T2D state. Especially, the analysis results suggest that the beta-cell heterogeneity identified in single-cell dataset may be smaller in T2D relative to a normal state; by contrast, the alpha cell shows an opposite effect.

Conclusions Along with the development of high-throughput single-cell sequencing technologies, we are now capable of investigating the T2D pathogenesis on each cell in addition to each individual. There are actually necessary requirements on investigating cellular heterogeneity underlying individual heterogeneity of T2D, for personalized diagnosis and prognosis of T2D.

IDDF2021-ABS-0200 BACILLUS AMYLOLIQUEFACIENS COMBINED WITH RESISTANT STARCH TO AMELIORATE INTESTINAL INFLAMMATION

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Background *Bacillus amyloliquefaciens* (BA) decomposes starch by producing alpha-amylase to produce short-chain fatty acids (SCFA). Resistant starch (RS) can be fermented by colonic microbiota and metabolized to SCFA containing acetic acid and butyric acid by which can ameliorate intestinal inflammation. In this study, dextran sulfate sodium (DSS)-induced colitis mouse model was administrated to assess the therapeutic effect of BA combined with RS in experimental colitis.

Methods 6-week-old male BALB/c mice were given 3% DSS drinking water for 1 week to induce acute colitis. Mice were fed with maintenance forage as control group. The content of RS was 465.692g/kg, and the abundance of BA by gavage administration in mice was 1×10^7 CFU for 7 days. The mice were administered daily, including weight loss and disease activity index (DAI). The mice were sacrificed on the eighth day. We collect specimens, measure colon length, evaluate histopathologic score and detect the level of IL-1 β , IL-6, TNF- α and occludin of intestinal tissue by qPCR.

Results Weight loss and DAI were more effectively improved in the live BA combined with RS than administered RS alone. Colonic inflammation was significantly alleviated in the live BA combined with RS. The colon length and histopathologic score of live BA combined with RS intervention were more improved than that of the control ($p < 0.001$), including a smaller extent of intestinal epithelial damage and crypt structure disorder. The degree of inflammatory cell infiltration was lighter ($p = 0.029$). The expression of IL-1 β ($p = 0.008$), IL-6 ($p = 0.02$) and TNF- α ($p < 0.001$) were reduced and the expression of Occludin ($p = 0.006$) was increased than RS alone.

Conclusions The intervention of BA combined with RS may ameliorate DSS-induced acute colitis and promote colon barrier recovery.